

## Case Report

# Recurrent respiratory papillomatosis with pulmonary cystic disease in a child, following maternal genital warts

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Human papillomavirus (HPV) infection of the genital tract is associated with the development of genital warts. A causal link between maternal HPV infection and development of laryngeal papillomatosis in the offspring has been proposed. We report a case of pulmonary cystic disease, a rare but serious complication of laryngeal papillomatosis in a child, following maternal genital warts.

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## Introduction

Laryngeal papillomata are benign tumours, most commonly occurring in infants and children. Although histologically benign, they can become a serious clinical problem because of their location, resistance to treatment, recurrences, and, rarely, due to their tendency to involve the lower respiratory tract.<sup>1</sup> It is now well established that respiratory papillomata are caused by HPV types 6 and 11.<sup>2,3</sup>

Genital warts occur in sexually active men and women, and are also caused by HPV types 6 and 11. A causal link between maternal condylomata and respiratory papillomatosis in the offspring has been proposed, and sporadic case reports have appeared describing this phenomenon.<sup>4</sup> We report the case of a young girl, with laryngeal papillomata and distal lung involvements, whose mother had genital warts at delivery.

## Case report

A 15 year old girl presented to the Chest Unit with a history of right sided pleuritic chest pain, productive cough and haemoptysis. Following a normal vaginal delivery at term, at the age of one year she had presented with dry cough, hoarseness of voice and stridor to the

ENT department. A diagnosis of laryngeal papillomatosis was made on laryngoscopy and histologically the papillomas proved to be benign. The severity of symptoms warranted a tracheostomy and subsequently she remained under the care of ENT surgeons, being treated with endoscopic laser therapy for recurrent papillomata. Her mother gave a history of having genital warts during pregnancy and delivery.

Physical examination of the girl revealed a tracheostomy tube with poor local hygiene. Chest examination was unremarkable. A chest radiograph showed multiple cysts with fluid levels. Routine blood tests were normal. Serum electrophoresis, alpha<sub>1</sub> antitrypsin levels, immunology studies (including T and B cell functions) were all normal. Sputum examination was negative for acid fast bacilli. Spirometry revealed a moderately severe combined obstructive and restrictive defect with FEV<sub>1</sub>/FVC of 1.1/2.2 (predicted 2.3/3.4), and arterial blood gases showed hypoxaemia with P<sub>O<sub>2</sub></sub> of 9.5 and pC<sub>O<sub>2</sub></sub> of 4.2. CT of the chest confirmed extensive cystic lesions in both lungs, most pronounced in the apices (fig).

It was concluded that the cysts were secondary to the laryngeal papillomas, and that her presenting symptoms were related to infec-

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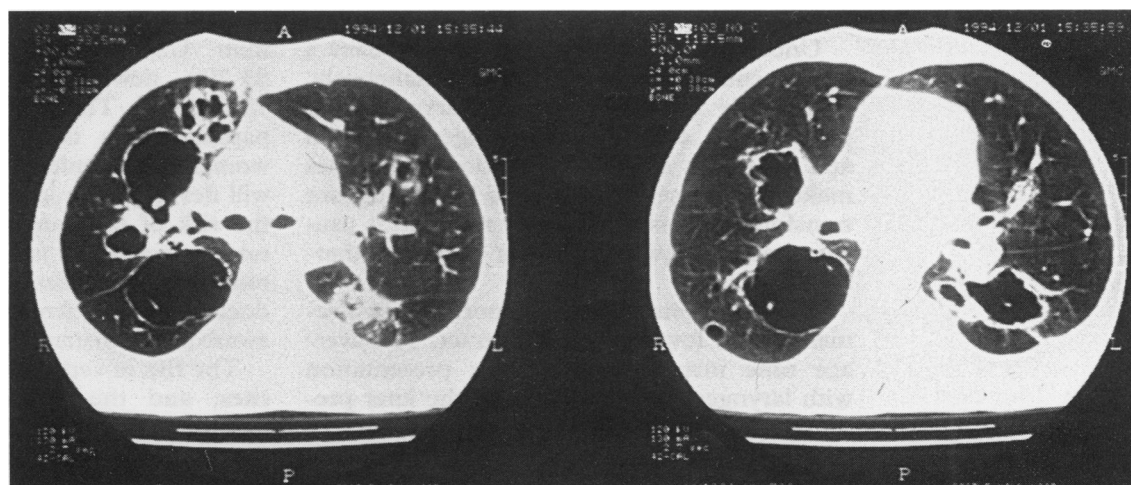
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CT scans of the chest.



tion within these cysts. With antibiotic treatment her symptoms abated, and the fluid levels within the cysts resolved.

A repeat of CT of the chest, a year later, showed significant deterioration of the lung cysts. Following this episode, her tracheostomy tube was blocked with new papillomata requiring several endoscopic resections. In situ hybridisation of these papillomata confirmed HPV11.

### Discussion

Laryngeal papillomata, the most common benign tumours of the larynx, were first described in the seventeenth century.<sup>5</sup> The term juvenile laryngeal papillomatosis prevailed in the 1960s; however, it is now clear that they can spread distally to involve the trachea in 2%, and lungs in 1% of cases.<sup>1</sup> The disease is notorious for its recurrence and hence is now termed "recurrent respiratory papillomatosis". Papillomata are relatively frequent in children, but can occur at any age. The highest incidence is before the age of 5 years.<sup>6</sup>

There is a strong evidence of viral aetiology. Batsakis postulated an activation of a persistent viral infection, coupled with an unknown promoter as the aetiological basis for laryngeal papillomata.<sup>2</sup> As yet no whole virus has been isolated from laryngeal papillomata but examination of DNA extracted from biopsy specimens has identified human papilloma virus types 6 and 11 as the aetiological agent.<sup>3</sup>

The link between maternal condylomata and respiratory papillomata in the offspring was proposed many years before the causal HPVs were shown to be identical. In 1956, Hajek reported a case of laryngeal papillomata in an infant born to a mother who had a history of extensive condylomata in late pregnancy and suggested that the disease was transmitted from the mother to the offspring during birth.<sup>4</sup> A history of maternal condylomata in pregnancy, or at the time of delivery, was elicited from 29% to 60% of mothers, of juvenile onset respiratory papillomatosis patients.<sup>7</sup> In contrast, such a history was obtained in less than 5% of obstetric patients.<sup>8,9</sup> The infection is usually acquired by the baby perinatally but rare instances of children with respiratory papillomata from caesarean delivery, have been reported.

Uncomplicated papillomata usually have a benign course and can regress spontaneously, particularly if confined to the larynx. Their potential to compromise laryngeal function and to cause airway obstruction sometimes makes them a serious threat to life. Malignant transformation is exceedingly rare and is usually associated with previous radiation therapy.

There are relatively few reports of involvement of the lower respiratory tract. The average time interval between the presentation with laryngeal papillomata, and the later presentation with cystic lung damage, is 12 years.<sup>5</sup> Patients with this complication have a poor prognosis, few surviving beyond the age

of 20.<sup>1</sup> Various theories have been proposed to explain the association, for example, contiguous extension of the papillomata, diffuse viral contamination, multicentric origin of papillomata, and aerial dissemination. Fragments can become detached during endoscopic resection and following tracheostomy, leading to distal spread.<sup>1</sup> Lung involvement can result in thin walled cysts, nodules, fibrosis and bronchiectasis. The mechanism of formation of lung cysts remains controversial. It may be due to obstruction of peripheral airways by the papilloma producing an area of emphysema by a check-valve mechanism, or it may result from necrosis and excavation of solid nodular lesion. The distribution and extent of lung lesions is best evaluated by CT.

As with other forms of HPV infection there is no treatment that will eradicate the virus. Numerous forms of medical and surgical treatment have been employed with varying success. Medical forms have included use of vaccine made from the patients papilloma, radiotherapy, ultrasound, injection of hormones, steroids, vidarabine, topical podophyllin, systemically administered calcium and magnesium, tetracyclines, topical or intralesional treatment with 5 fluorouracil, systemic bleomycin and human leucocyte interferon.<sup>10</sup> The mainstay of palliation is endoscopic resection. A single removal is occasionally curative but recurrence commonly requires further intervention. In recent years microsurgical techniques and the use of carbon dioxide laser treatment has been advocated.<sup>9</sup> Tracheostomy is avoided if at all possible. The variety of treatments employed in the management demonstrate that there is no known cure, and attempts to prevent recurrence have been largely unsuccessful.

Cystic pulmonary lesions in themselves are rarely symptomatic and require no treatment unless infected. Death is usually associated with complications of a surgical procedure or respiratory failure, due to disease progression and loss of pulmonary parenchyma. If therapeutic HPV vaccines prove successful in the treatment of genital warts, they may offer a further therapeutic option for recurrent respiratory papillomatosis. This may also raise the possibility of lung transplantation in patients with parenchymal lung damage, as in the case described.

HPV infection of the genital tract is common. USA national figures have estimated 85 200 new cases of genital warts in 1993–1994. The best estimate of the risk of papillomatosis is 1 in 400 pregnancies of women with genital warts. Only 1% of these will develop lung involvement. In light of this the risk of pulmonary papillomatosis is very rare, however as it is a serious condition with a reduced life expectancy, it is important that doctors treating women with genital warts are aware of its existence.

The risk of vertical spread to infant mucosal sites, and the seriousness of laryngeal to pulmonary transmission at a later stage, as in the case we have described, needs to be emphasised.

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